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Editorial

Highlights from the 5th International Conference on Vitamin D Deficiency, Nutrition and Human Health, Abu Dhabi, United Arab Emirates, March 24–25, 2016

Abu Dhabi is the venue for a series of annual vitamin D conferences conducted since 2012. The 5th International Vitamin D Conference was held in Abu Dhabi on March 24–25, 2016. In this special issue 25 papers were accepted for publication.

The first day of the conference started with the keynote lecture by Dr. Carsten Carlberg (University of Eastern Finland, Kuopio, Finland) on the genome-wide role of vitamin D. In this context the concept of the personal vitamin D response index was described [1]. This concept is based on the fact that vitamin D_3 activates via its metabolite 1,25-dihydroxyvitamin D_3 the transcription factor vitamin D receptor (VDR) and thus has a direct effect on the epigenome and transcriptome of those human tissues and cell types that express the receptor. The efficiency and strength of the molecular response to vitamin D supplementation varies between individuals and can be measured during vitamin D intervention trials. Dr. Carlberg suggested that this personal vitamin D response index should be taken into account in addition to traditional measurements of the vitamin D status via serum levels of the most stable vitamin D metabolite, 25-hydroxyvitamn D_3 ($25(OH)D_3$).

The following four presentations were related with the epidemiology of vitamin D deficiency covering $25(OH)D_3$ levels in population living in the United Arab Emirates (UAE), Saudi Arabia, Kuwait and Portugal. Dr. Afrozul Haq (Founding President of the International Vitamin D Conference) reported on juvenile population living in the UAE [2]. He demonstrated that 82.5% of the study cohort (7883 patients, aged 1–18) had vitamin D insufficiency as defined by a serum $25(OH)D_3$ level below 75 nM. 58.1% of females and 43.3% of males even showed $25(OH)D_3$ levels below 50 nM. Vitamin D deficiency ($[25(OH)D_3] < 30$ nM) was observed in 31.4% of patients in the age group of 10–12 years, in 50.4% of the 13–15 years old and even in 52.9% of the 16–18 years old. Dr. Nasser Al-Daghri (King Saud University, Riyadh, Saudi Arabia) reviewed recent (2011–2016) vitamin D studies from Saudi Arabia and revealed that the prevalence of a low vitamin D status ($[25(OH)D_3] < 50$ nM) among different populations (adults, children and adolescents, newborns and pregnant/lactating women) is 81% [3]. This is in line with most neighboring Gulf countries. Drs. Deena Elsori and Majeda Hammoud presented the vitamin D status of mothers, neonates and children from Kuwait. They showed that increased rates of gestational diabetes among pregnant women, low birth weight of infants and pre-clampsia in mothers result in bone impairment, osteoporosis, hypocalcemia and hypertension [4]. Dr. Bettencourt and colleagues reported on the vitamin D status of the healthy population from north of Portugal. The mean $25(OH)D_3$ serum level of all 198 investigated individuals (18–67 years) was 55.4 ± 23.4 nM, with 48% of them being below 50 nM. In the winter period this value even reached 74%. No statistically significant differences were observed between genders or between age and $25(OH)D_3$ levels [5].

In two papers Dr. Haq and Dr. Pawel Pludowski (Children's Memorial Health Institute, Warsaw, Poland) discussed vitamin D guidelines in the UAE [6] and in Europe [7]. They recommended vitamin D_3 supplementation of (i) breastfed infants with 400 IU/day up to age 6 months and 400–600 IU/day between 6 and 12 months, depending on daily intake of total vitamin D and sun exposure, (ii) children and adolescents (1–18 years) with 600–1000 IU/day depending on the body weight, (iii) adults with 1000–2000 IU/day, (iv) the elderly (over 65 years) with 2000 IU/day throughout the year, (v) pregnant and breast feed women with 2000 IU/day from the first trimester of pregnancy, (vi) premature infants with 400–800 IU/day start from the first days of life, (vii) obese individuals and those with metabolic syndrome with 2000 IU/day, (viii) individuals with dark skin and night workers with 1000–2000 IU/day throughout the year depending on body weight. The goal of supplementation is to achieve and maintain a vitamin D status of 75–125 nM. Dr. Pludowski emphasized that (i) vitamin D supplementation is crucial for both classic and pleiotropic effects, (ii) serum $25(OH)D_3$ concentrations of 75–125 nM are beneficial for overall health, (iii) regional or nationwide vitamin D guidelines are more applicable for general population and (vi) disease-specific vitamin D guidelines are applicable globally.

A paper by Drs. John Cannell and Michael Holick discussed multiple unexplained fractures in infants and child/physical abuse [8]. The key points of their study were that (i) radiologists miss biopsy proven rickets in 80% of the time, (ii) common sense issues must be considered in child abuse, not just X-rays, (iii) infantile rickets may be very common (to date no one has studied its prevalence) and (iv) it is possible that an ultrasound study of newborns will be very informative.

Dr. Vin Tangpricha (Emory University, Atlanta, USA) presented the association between vitamin D deficiency and the redox potential of oxidized plasma cysteine in critically ill children in a cross-sectional study in pediatric intensive care unit patients [9]. Vitamin D sufficiency was associated with a decreased redox potential of plasma cysteine indicating lower oxidative stress in critically ill children. Dr. Tangpricha concluded that there is a link between vitamin D, oxidative stress and immunity. Dr. Mohammed Razzaque (Harvard University, Cambridge, USA) explained in his presentation that hypovitaminosis D usually reflects reduced sunlight exposure. Therefore, the obvious primary replacement should be safe sunlight

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exposure, and not exogenous supplements [10]. Dr. Shereen Atef (National Research Laboratory, Abu Dhabi, UAE) compared different assays for measuring the vitamin D status, such as chemiluminescence immunoassays (CLIA), radioimmunoassay (RIA), high performance liquid chromatography (HPLC) and liquid chromatography–tandem mass spectrometry (LC–MS/MS) [11]. Significant differences were observed between various assays. Thus, standardization and harmonization of 25(OH)D_3 measurements are urgently needed.

In his second presentation Dr. Razzaque focused on the impact of vitamin D on oral health [12]. The beneficial effects of vitamin D on oral health are not only limited to the direct effects on the tooth mineralization, but are also exerted through the anti-inflammatory functions and the ability to stimulate the production of anti-microbial peptides. Dr. Sunil Wimalawansa (Cardio Metabolic Institute, Somerset, NJ, USA) presented correlations between non-musculoskeletal disorders and the vitamin D status [13]. Serum 25(OH)D_3 levels less than 50 nM, i.e. a low vitamin D status, are associated with increased morbidity, myocardial infarction and all-cause mortality. Therefore, most professional societies recommend in the absence of sufficient sun exposure a daily supplementation with 1000–2000 IU vitamin D_3, in order to reach serum 25(OH)D_3 levels between 75 and 125 nM.

Furthermore, Dr. Wimalawansa reviewed the possible causality of vitamin D deficiency and cardiovascular diseases (CVDs) [14]. Randomized controlled trials (RCTs) indicate that vitamin D has beneficial effects on CVD. An optimal vitamin D status facilitating beneficial pleiotropic effects, such as CVDs, seems to be 25(OH)D_3 serum levels of 75–150 nM. However, there are no long-term, adequately powered, randomized clinical studies with vitamin D available that have CVD as the primary endpoint. Grübler and colleagues reported on a RCT, in which 200 patients with atrial hypertension and vitamin D insufficiency ([25(OH)D_3] $<$ 75 nM) were daily supplemented for 8 weeks with either 2800 IU vitamin D_3 or placebo. While there were no significant treatment effects of the whole group, a subgroup with vitamin D deficiency ([25(OH)D_3] $<$ 50 nM) showed a significant increase in their arginine/asymmetric dimethylarginine ratio [15].

In his metabolically oriented presentation Dr. Wimalawansa pointed out that a low vitamin D status correlates with overweight, abdominal obesity and the occurrence of stroke [16]. Cross-sectional studies reported an inverse association between vitamin D status and hyperglycemia and seasonal variation of glycemic control in patients with type 2 diabetes (T2D). Moreover, observational studies suggested that a low vitamin D status is associated with increased risk for pre-diabetes, T2D and the metabolic syndrome. However, RCTs provide only little evidence concerning optimal serum 25(OH)D_3 levels for the prevention of such complications. Karonova and colleagues reported on a higher prevalence of vitamin D deficiency and low serum adipokine levels in individuals with abdominal obesity that was independent of gender [17]. Serum 25(OH)D_3 levels inversely correlated with weight, waist circumference and body mass index in females but not in males. Similarly, a significant correlation between leptin and serum 25(OH)D_3 levels was found only in females. Dr. Fatme Al Anouti (Khalifa University, Abu Dhabi, UAE) highlighted in her presentation that the UAE population has one of the highest rates of T2D worldwide. Dr. Al Anouti presented data on *VDR* gene polymorphisms among Emirati patients and suggested that *VDR* alleles and haplotypes as candidates for T2D susceptibility [18].

A report from Dr. John White describes the correlation of vitamin D deficiency and Crohn's disease, which is a relapsing-recurring inflammatory bowel disease [19]. Intervention trials provided solid evidence that vitamin D supplementation is of therapeutic benefit to patients with the disease. Mechanistically the effects of vitamin D can be explained via its important gene regulatory functions in cells of the innate immune system. Along the same lines a review by Dr. Mansi Kanhere and colleagues discusses the favorable role of vitamin D in altering the gut microbiota, in order to control intestinal inflammation [20]. Cystic fibrosis patients often display vitamin D deficiency due to gut mal-absorption and an altered composition of intestinal microbiota. Vitamin D maintains the integrity of the gut mucosal barrier and modulates the expression of pro-inflammatory cytokines, such as IL8. Thus, a sufficient vitamin D status is essential for the development of a healthy gut microbiota, particularly in conditions defined by chronic mucosal inflammation. Two original publications by Dr. David Jolliffe and colleagues report on the prevalence, determinants and clinical correlates of vitamin D deficiency in healthy adults and patients, respectively, with inhaled corticosteroid-treated asthma [21,22]. In both groups the vitamin D status did not associate with any studied marker of asthma severity. This is in contrast to studies conducted in children.

Dr. Nighat Sofi gave a presentation on nutritional risk factors and the vitamin D status of breast cancer patients in India [23]. In a study of 100 women with breast cancer and 100 healthy females, cancer cases occurred more likely in less frequent fruits consumers and less likely with mushroom consumers. Saturated fat intake and high waist-to-hip ratio significantly associated with high risk for breast cancer. The majority of the patients with breast cancer have a low vitamin D status, which is significantly associated with the disease. Obesity, as expressed by a higher waist-to-hip ratio, was found to be significantly associated with the risk of breast cancer.

Dr. Pauline Lemire and colleagues report on the effect of memantine, a drug for the symptomatic treatment of Alzheimer's disease, in relation to the vitamin D status of the patients [24]. The use of memantine was associated with improved cognitive performance after 6 months of treatment in the presence of vitamin D deficiency. Thus, memantine may prevent the cognitive decline that accompanies the onset of vitamin D deficiency, suggesting that Alzheimer patients should receive memantine in combination with vitamin D_3 supplementation. Finally, Dr. Asad Ali and colleagues summarized current knowledge on autism and vitamin D deficiency during development [25]. 1,25-dihydroxyvitamin D_3 is an active neurosteroid and plays crucial neuroprotective roles in the developing brain. As vitamin D deficiency is emerging in children, it may also a risk factor for autism. The potential neurobiological mechanisms linking prenatal vitamin D deficiency and autism are discussed in this review.

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